IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: MARSHALL, WILLIAM E.	)
	) **APPEAL NO.** _____
SERIAL NO: 09/883,550	)
	)
FOR: METHODS AND COMPOSITIONS FOR MODULATING IMMUNE SYSTEMS OF ANIMALS	) **BRIEF ON APPEAL**
	)
FILED: JUNE 18, 2001	)
	)
GROUP ART UNIT: 1638	)

To Commissioner for Patents
Mail Stop Appeal Brief – Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs and Madams:

In response to the Notification of Non-Compliant Appeal Brief dated December 5, 2006, please find attached a revised summary of the claimed matter for the above-identified appeal brief. Applicants believe that they are in compliance with 37 CFR 41.37(c)(1)(v) and request that this be entered.

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JANAE E. LEHMAN BELL, Ph.D.

Respectfully submitted,

Jmaé E. Lehman Bell, Ph.D., Reg. No. 55,370
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338

Attorneys of Record

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V. SUMMARY OF CLAIMED SUBJECT MATTER

This invention relates to methods and compositions for modulating immune responses of animals or humans. (*See* Original specification as filed, p. 9, ll. 15-34, and p. 10, ll. 1-19). More particularly, the invention relates to methods of modulating immune responses of animals or humans by administering effective amounts of a partially purified composition prepared from a mixture released by the stressing of bacteria after they have been grown under specified conditions. (*See* Original specification as filed, p. 11, l. 6 – p. 12, l. 28; p. 21, l. 1 – p. 22, l. 12). This composition includes stress response factors that activate and modulate circulating macrophages. (*See* Original specification as filed, p. 1, ll. 27–33; p. 19, l. 1 – p. 20, l. 20).

The present inventors have found that the stress-response-factors (SRFs), between 0.5 and 10. kDa are a rich new source of natural, normally-occurring, co-evolutionarily evolved immune modulators that can be safely used to protect animals and humans from infections and over-stimulation of their immune system. (*See* Original specification as filed, p. 21, l. 1– p.22, l. 14).

The present inventor has discovered that SRFs that modulate the immune system may be created by growing bacteria in a medium and exposing said bacteria to biological, chemical or physical stress for at least two or more sequential periods of stress of approximately 20 minutes or less. (*See* Original specification as filed, p. 11, l. 6 – p. 12, l. 28). The inventor has discovered that the bacteria after such stressing release a stress response product comprising stress response factors (SRFs) into the medium. (*See* Original specification as filed, p. 12, ll. 10-28). These SRFs are then separated from the medium to form a separated product. (*See* Original specification as filed, p. 12, l. 29 – p.

13, l. 4). The separated product is then filtered to remove substances having a molecular weight of greater than 10kDa to form a filtrate. (*See* Original specification as filed, p. 12, l. 29 – p. 13, l. 4). The resulting filtrate of less than 10kDa can then be administered to animals. (*See* Original specification as filed, p. 13, l. 34 – p. 14, l. 3).

This fraction was shown in cell cultures to induce the release of cytokines, IL-1, IL-6, and TNFα and decrease the expression of individual surface receptors CD-14 and CD-16 on macrophages, thereby re-centering a dysfunctional immune system and desensitizing it to a subsequent lethal challenge of injected endotoxin, LPS. (*See* Original specification as filed, p. 19, l. 1– p. 22, l. 14). Furthermore, in vitro testing indicates their potential role as adjuvants by stimulating the release of IL-12. (*See* Original specification as filed, p. 5, ll. 13-15).

An additional discovery is the finding that feral colonies of bacteria yield more oligomeric SRFs than non-feral or laboratory strains. (*See* Original specification as filed, p. 5, ll. 15-18). However, after stressing, laboratory strains assume the more robust growth characteristics of feral strains and the subsequent release of more SRFs when stressed. (*See* Original specification as filed, p. 5, ll. 19-22). The release of SRFs can be tracked by measuring their peak of absorption at 254 nm that typically is associated with nucleotides. (*See* Original specification as filed, p. 16, l. 23 – p.17, l. 14, p. 12, ll. 29-31).

The discovery of the release of immune-activating and modulating factors has broad implications to improving the immune response through diets and pharmaceutical preparations for humans and animals. (*See* Original specification as filed, p. 5, ll. 23-26). Products, e.g. milk, cheese, yogurts contain viable bacteria, which, when transferred to the nutrient deprived and pH neutral environment of the mouth release SRFs. (*See*

Original specification as filed, p. 5, ll. 26-28). If such products were formulated to extend the dwell-time in the mouth, more SRFs would be released, activating and modulating a greater local immune response. (*See* Original specification as filed, p. 5, ll. 29-31). Material relevant to the appealed claims is described throughout the Specification.